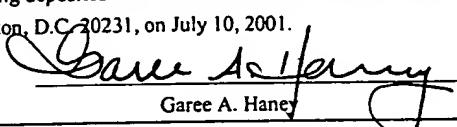




PATENT
Docket No. 432722002623

CERTIFICATE OF MAILING BY "FIRST CLASS MAIL"

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:
Assistant Commissioner for Patents, Washington, D.C. 20231, on July 10, 2001.


Garee A. Haney

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Gregory R. MUNDY et al.

Serial No.: 09/695,807

Filing Date: October 23, 2000

For: INHIBITORS OF PROTEASOMAL
ACTIVITY FOR STIMULATING BONE
AND HAIR GROWTH

Examiner: To Be Assigned

Group Art Unit: 1646

INFORMATION DISCLOSURE
STATEMENT UNDER 37 C.F.R. § 1.97

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to 37 C.F.R. § 1.97 and § 1.98, Applicants submit for consideration in the above-identified application the documents listed on the attached Form PTO-1449. Copies of the documents Nos. 1, 10, 55, 63, 68 and 76, are included herewith. Copies of all other documents were previously submitted in an Information Disclosure Statement and/or Office Action, directed to the related application Serial Numbers 09/558,973, filed April 25, 2000, 09/421,545, filed October 20, 1999, 09/361,775, filed July 27, 1999, and 09/113,947, filed July 10, 1998, and accordingly, copies are not included herewith. This protocol conforms with 37 C.F.R. § 1.98(d)

4542

and M.P.E.P. 609(A)(2). The Examiner is requested to make these documents of record. Applicants bring to the examiner's attention serial number 08/458,434, cited in the above-identified application which has since been granted and is now U.S. Patent 6,083,690. Accordingly, a copy of the granted patent is submitted herewith.

This Information Disclosure Statement is submitted:

- With the application; accordingly, no fee or separate requirements are required.
- Within three months of the application filing date or before mailing of a first Office Action on the merits; accordingly, no fee or separate requirements are required.
- After receipt of a first Office Action on the merits but before mailing of a final Office Action or Notice of Allowance.
 - A fee is required. A check in the amount of * is enclosed.
 - A fee is required. Accordingly, a Fee Transmittal form (PTO/SB/17) is attached to this submission in duplicate.
 - A Certification under 37 C.F.R. § 1.97(e) is provided below; accordingly; no fee is believed to be due.
- After mailing of a final Office Action or Notice of Allowance, but before payment of the issue fee. Accordingly, a Petition requesting consideration of the Information Disclosure Statement, an authorization to charge our deposit account, and a Certification under 37 C.F.R. § 1.97(e) are provided herein.

Applicants would appreciate the Examiner initialing and returning the Form PTO-1449, indicating that the information has been considered and made of record herein.

The information contained in this Information Disclosure Statement under 37 C.F.R. § 1.97 is to the best of my knowledge and is not to be construed as a representation

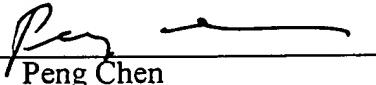
that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing 432722002623. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: July 10, 2001

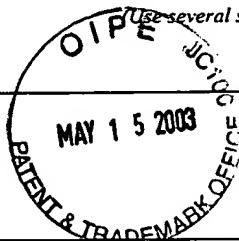
Respectfully submitted,

By:


Peng Chen
Registration No. 43,543

Morrison & Foerster LLP
3811 Valley Centre Drive
Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-5117
Facsimile: (858) 720-5125

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>	Docket Number 432722002623	Application Number 09/695,807
	Applicant Gregory R. MUNDY <i>et al.</i>	
	Filing Date October 23, 2000	Group Art Unit 1646
	Mailing Date July 10, 2001	



U.S. PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Name	Class	Subclass	Filing Date If Appropriate
1.			09/096,631				June 12, 1998
2.	8/1988		4,761,471	Urist	530	350	
3.	1/1994		5,280,040	Labroo <i>et al.</i>	514	457	
4.	12/1996		5,580,854	Orlowski <i>et al.</i>	514	18	
5.	3/1998		5,728,844	Muller <i>et al.</i>	548	472	
6.	6/1998		5,767,152	Nielsen <i>et al.</i>	514	526	
7.	7/1998		5,780,454	Adams <i>et al.</i>	514	64	
8.	10/1998		5,824,643	Pierce <i>et al.</i>	514	12	
9.	6/1999		5,910,497	Durette <i>et al.</i>	514	253	
10.	7/2000		6,083,690	Harris <i>et al.</i>	435	6	

FOREIGN PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Country	Class	Subclass	Translation YES NO
	11.	10/1990	WO 90 11366	WIPO			
	12.	3/1992	WO 92 03125	WIPO			
	13.	10/1993	WO 93 20859	WIPO			
	14.	9/1995	WO 95 24211	WIPO			
	15.	9/1995	WO 95 25533	WIPO			
	16.	12/1996	WO 96 38590	WIPO			
	17.	3/1997	WO 97 09315	WIPO			
	18.	5/1997	WO 97 15308	WIPO			
	19.	7/1997	WO 97 23457	WIPO			
	20.	10/1997	WO 97 38699	WIPO			
	21.	12/1997	WO 97 48694	WIPO			
	22.	4/1998	WO 98 17267	WIPO			
	23.	6/1998	WO 98 25460	WIPO			

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

#46693

MAY 15 2003
PATENT & TRADEMARK OFFICE

Form PTO-1449

INFORMATION DISCLOSURE CITATION
IN AN APPLICATION

(Use several sheets if necessary)

Docket Number 432722002623	Application Number 09/695,807
Applicant	Gregory R. MUNDY <i>et al.</i>
Filing Date October 23, 2000	Group Art Unit 1646
Mailing Date July 10, 2001	

24.	1/2000	WO 0002548	WIPO				
25.	10/1998	DE 197 16 713	Germany				
26.	7/1999	EP 0 931 544	Europe				
27.	4/1993	JP 05 097697	Japan				

OTHER DOCUMENTS

(including author, title, Date, Pertinent Pages, Etc.)

Examiner Initials	Ref. No.	Title
	28.	Abu-Amer <i>et al.</i> , "NF- κ B and Bone: The Breaking Point," NATURE MEDICINE (1997) 3(11):1189-1190
	29.	Adams, J. <i>et al.</i> , "Proteasome Inhibitors: A Novel Class of Potent and Effective Antitumor Agents," CANCER RES (1999) 59:2615-2622
	30.	Adams <i>et al.</i> , "Chapter 28. Novel Inhibitors of the Proteasome and their Therapeutic Use in Inflammation," ANNUAL REPORTS IN MEDICINAL CHEMISTRY (1996) 279-288
	31.	Ahmed <i>et al.</i> , "Alopecia Universalis Associated with a Mutation in the Human Hairless Gene," SCIENCE (1998) 279:720-724
	32.	Bangham <i>et al.</i> , "Diffusion of Univalent Ions Across the Lamellae of Swollen Phospholipids," J MOL BIOL (1965) 23:238-252
	33.	Barnes <i>et al.</i> , "Nuclear Factor - κ B - A Pivotal Transcription Factor in Chronic Inflammatory Diseases," NEW ENGL J MED (1997) 336:1066-1071
	34.	Baumeister <i>et al.</i> , "The Proteasome:Paradigm of a Self-Compartmentalizing Protease," CELL(1998) 92:367-380
	35.	Beck <i>et al.</i> , "Rapid Publication TGF- β ₁ Induces Bone Closure of Skull Defects," J BONE MINER RES (1991) 6(11):1257-1265
	36.	Bellows <i>et al.</i> , "Determination of the Capacity for Proliferation and Differentiation of Osteoprogenitor Cells in the Presence and Absence and Absence of Dexamethasone," DEVELOP BIOL (1990) 140:132-138
	37.	Blessing <i>et al.</i> , "Transgenic Mice as a Model to Study the Role of TGF- β -Related Molecules in Hair Follicles," GENES AND DEVELOP (1992) 7:204-215
	38.	Burgener <i>et al.</i> , "Fluoride Increase Tyrosine Kinase Activity in Osteoblast-like Cells: Regulatory Role for the Stimulation of Cell Proliferation and Pi Transport Across the Plasma Membrane," J BONE MINER RES (1995) 10:164-171
	39.	Caplan, "Mesenchymal Stem Cells" J ORTHOP RES (1991) 9:641-650
	40.	Casez <i>et al.</i> , "Dual-Energy X-Ray Absorptiometry for Measuring Total Bone Mineral Content in the

EXAMINER:	DATE CONSIDERED:
EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.	

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>		Docket Number 432722002623	Application Number 09/695,807
		Applicant	Gregory R. MUNDY <i>et al.</i>
		Filing Date October 23, 2000	Group Art Unit 1646
		Mailing Date July 10, 2001	

	Rat: Study of Accuracy and Precision," BONE AND MINER (1994) 26:61-68		
41.	Combaret, L. <i>et al.</i> , "Manipulation of the Ubiquitin-Proteasome Pathway in Cachexia: Pentoxyfylline Suppresses the Activation of 20S and 26S Proteasomes in Muscles from Tumor-Bearing Rats," MOL BIOL REP (1999) 26:95-101		
42.	Coux, O. <i>et al.</i> , "Structure and Functions of the 20S and 26S Proteasomes," AN REVIEW BIOCHEM (1996) 65:801-847		
43.	Craiu, A. <i>et al.</i> , "Lactacystin and Clasto-Lactacystin β -Lactone Modify Multiple Proteasome β -Subunits and Inhibit Intracellular Protein Degradation and major Histocompatibility Complex Class I Antigen Presentation," J BIOL CHEM (1997) 272:13437-13445		
44.	Cui <i>et al.</i> , "Lovastatin Prevents Steroid-Induced Adipogenesis and Osteoporosis," ASBMR 18th Annual Meeting (September 1996) J BONE MINER RES (1996) 11(S1):S510		
45.	Ducy <i>et al.</i> , "Increased Bone Formation in Osteocalcin-deficient Mice," NATURE (1996) 382:448-452		
46.	Edelman <i>et al.</i> , "Controlled and Modulated Release of Basic Fibroblast Growth Factor," BIOMATERIALS (1991) 12:619-626		
47.	Elofsson <i>et al.</i> , Chemistry & Biology (1999) 6:811-822		
48.	Ferretti, "Perspectives of pQct Technology Associated To Biomechanical Studies in Skeletal Research Employing Rat Models," BONE (1995) 17:353S-364S		
49.	Figueiredo-Pereira <i>et al.</i> , "A New Inhibitor of the Chymotrypsin-Like Activity of the Multicatalytic Proteinase Complex (20S Proteasome) Induces Accumulation of Ubiquitin-Protein Conjugates in a Neuronal Cell," J NEUROCHEM (1994) 63:1578-1581		
50.	Franzoso <i>et al.</i> , "Requirement for NF- κ B in Osteoclast and B-Cell Development," GENES AND DEV (1997) 11:3482-3496		
51.	Garrett <i>et al.</i> , "Specific Inhibitors of the Chymotryptic Component of the Proteasome are Potent Bone Anabolic Agents In Vivo" Journal of Bone and Mineral Research (2000) 15(Suppl.1):S197		
52.	Gat <i>et al.</i> , "De Novo Hair Follicle Morphogenesis and Hair Tumors in Mice Expressing a Truncated β -Catenin in Skin," CELL (1998) 95:605-614		
53.	Ghosh-Choudhury <i>et al.</i> , "Immortalized Murine Osteoblasts Derived from BMP 2-T-Antigen Expressing Transgenic Mice," ENDOCRINOLOGY (1996) 137:331-339		
54.	Gowan <i>et al.</i> , "Actions of Recombinant Interleukin 1, Interleukin 2, and Interferon- γ on Bone Resorption in Vitro," J IMMUNOL (1986) 136:2478-2482		
55.	Groll <i>et al.</i> , J. Am. Chem. Soc. (2000) 122:1237-1238		
56.	Guirarro <i>et al.</i> , "Lovastatin Inhibits Lipopolysaccharide-induced NF- κ B Activation in Human Mesangial Cells," NEPHROL DIAL TRANSPLANT (1996) 11:990-996		
57.	Gupta <i>et al.</i> , "Oral Cyclosporine for the Treatment of Alopecia Areata," J AMER ACAD OF DERMATOLOGY (1990) 22(2):242-250		

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

Form PTO-1449

INFORMATION DISCLOSURE CITATION
IN AN APPLICATION

(Use several sheets if necessary)

MAY 15 2003

Docket Number 432722002623

Application Number 09/695,807

Applicant

Gregory R. MUNDY *et al.*

Filing Date October 23, 2000

Group Art Unit 1646

Mailing Date July 10, 2001

PATE SPE SERIAL NUMBER	58.	Hardy <i>et al.</i> , "The Secret Life of the Hair Follicle," TRANS GENET (1992) 8:55-61
	59.	Harris <i>et al.</i> , "Effects of Transforming Growth Factor β on Bone Nodule Formation and Expression of Bone Morphogenetic Protein 2, Osteocalcin, Osteopontin, Alkaline Phosphatase, and Type I Collagen mRNA in Long-Term Cultures of Fetal Rat Calvarial Osteoblasts," J BONE MINER RES (1994) 9:855-863
	60.	Hilt, W. <i>et al.</i> , "Proteasomes: Destruction as a Programme," TRANS BIOCHEM SCI 91996) 21:96-101.
	61.	Iotsova <i>et al.</i> , "Osteopetrosis in Mice Lacking NF- κ B1 and NF- κ B2," NATURE MED (1997) 3:1285-1289
	62.	Jensen, T.J. <i>et al.</i> , "Multiple Proteolytic Systems, Including the Proteasome, Contribute to CFTR Processing," CELL (1995) 83:129-135
	63.	Kamiya <i>et al.</i> , J. Derm. Sci. (1998) 17:54-60
	64.	Kim <i>et al.</i> , "Preparation of Multivesicular Liposomes," BIOCHIM BIOPHYS ACTA (1983) 728:339-348
	65.	Kimmel <i>et al.</i> , "The Effect of Recombinant Human (1-84) or Synthetic Human (1-34) Parathyroid Hormone on the Sleton of Adult Osteopenic Ovariectomized Rats," ENDOCRINOLOGY (1993) 132:1577-1584
	66.	Ksander <i>et al.</i> , "Exogenous Transforming Growth Factor-Beta 2 Enhances Connective Tissue Formation and Wound Strength in Guinea Pig Dermal Wounds Healing by Secondary Intent," ANN SURG (1990) 211(3):288-294
	67.	Laval-Jeantet <i>et al.</i> , "Dual-EnergyX-Ray Absorptiometry of the Calcaneus: Comparison with Vertebral Dual-Energy X-Ray Absorptiometry and Quantitative Computed Tomography," CALCIF TISSUE INTL (1995) 56:14-18
	68.	Law <i>et al.</i> , Mol. Cell Biol. (1992) 12:103-111
	69.	Leserman <i>et al.</i> , "Targeting to Cells of Fluorescent Liposomes Covalently Coupled With Monoclonal Antibody or Protein A," NATURE (1980) 288:602-604
	70.	Liptay <i>et al.</i> , "Inhibition of Nuclear Factor Kappa B and Induction of Apoptosis in T-Lymphocytes by Sulfasalazine," BR J PHARMACOL (1999) 128(7):1361-1369
	71.	Lutz, "Effects of Cyclosporin A on Hair," SKIN PHARMACOLOGY (1994) 7:101-104
	72.	Majeska <i>et al.</i> , "Maintenance of Parathyroid Hormone Response in Clonal Rat Osteosarcoma Lines," EXP CELL RES (1978) 111:465-467
	73.	Maupin-Furlow, J.A. <i>et al.</i> , "A Proteasome from the methanogenic Archaeon Methanosaeca thermophila," J BIOL CHEM (1995) 270:28617-28622
	74.	Mayer <i>et al.</i> , "Vesicles of Variable Sizes Produced by a Rapid Extrusion Procedure," BIOCHIM BIOPHYS ACTA (1986) 858:161-168
	75.	Meng <i>et al.</i> , "Epoxomicin, a Potent and Selective Proteasome Inhibitor, Exhibits In Vivo

EXAMINER:

DATE CONSIDERED:

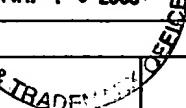
EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

Form PTO-1449

INFORMATION DISCLOSURE CITATION
IN AN APPLICATION

(Use several sheets if necessary)

MAY 15 2003



Docket Number 432722002623	Application Number 09/695,807
Applicant	Gregory R. MUNDY <i>et al.</i>
Filing Date October 23, 2000	Group Art Unit 1646
Mailing Date July 10, 2001	

	Antiinflammatory Activity" Proceedings of the National Academy of Sciences of the United States (1999) 96(18):10403-10408
76.	Mundy <i>et al.</i> , Science (1999) 286:1946-1949
77.	Murray <i>et al.</i> , "The Ubiquitin-Proteasome System and Cellular Proliferation and Regulation in Osteoblastic Cells," EXPERIMENTAL CELL RESEARCH (1998) 242:460-469
78.	Olson <i>et al.</i> , "Preparation of Liposomes of Defined Size Distribution by Extrusion Through Polycarbonate Membranes," BIOCHIM BIOPHYS ACTA (1979) 557:9-23
79.	Orford <i>et al.</i> , "Serine Phosphorylation-Regulated Ubiquitination and Degradation of β -Catenin," J BIOL CHEM (1997) 272:24735-24738
80.	Ozaki <i>et al.</i> , "NF- κ B Inhibitors Stimulate Apoptosis of Rabbit Mature Osteoclasts and Inhibit Bone Resorption by these Cells," FEBS LETTERS (1997) 410:297-300
81.	Pahl <i>et al.</i> , "The Immunosuppressive Fungal Metabolite Gliotoxin Specifically Inhibits Transcription Factor NF- κ B," J EXP MED (1996) 183:1829-1840
82.	Patent Abstracts of Japan (August 12, 1993) 17:436 (C-1096)
83.	Patent Abstracts of Japan (June 20, 1987) 11:193 (C-430)
84.	Patent Abstracts of Japan (April 25, 1986) 10:112 (C-342)
85.	Peters, J. "Proteasomes: Protein Degradation Machines of the Cell," TRENDS BIOCHEM SCI (1994) 19: 377-382
86.	Rickard <i>et al.</i> , "Induction of Rapid Osteoblast Differentiation in Rat Bone Marrow Stromal Cell Cultures by Dexamethasone and BMP-2," DEVELOP BIOL (1994) 161:218-228
87.	Sampath <i>et al.</i> , "Isolation of Osteogenin, an Extracellular Matrix-Associated, Bone-Inductive Protein, by Heparin Affinity Chromatography," PROC NATL ACAD SCI USA (1987) 84:7109-7113
88.	Sin, N. <i>et al.</i> , "Total Synthesis of the Potent Proteasome Inhibitor Epoxomicin: A Useful Tool for Understanding Proteasome Biology," BIORG MED CHEM LETT (1999) 9:2283-2288
89.	Szoka <i>et al.</i> , "Procedure for Preparation of Liposomes With Large Internal Aqueous Space and High Capture by Reverse-Phase Evaporation," PROC NATL ACAD SCI USA (1978) 75:4194-4198
90.	Tencer <i>et al.</i> , "The Effect of Local Controlled Release of Sodium Fluoride on the Stimulation of Bone Growth," J BIOMED MAT RES (1989) 23:571-589
91.	Vinitsky <i>et al.</i> , "Inhibition of the Proteolytic Activity of the Multicatalytic Proteinase Complex (Proteasome) by Substrate-Related Peptidyl Aldehydes," J BIOL CHEM. (1994) 269(47):29860-29866
92.	Wahl <i>et al.</i> , "Sulfasalazine: A Potent and Specific Inhibitor of Nuclear Factor Kappa B," J CLIN INVEST (1998) 101(5):1163-1174
93.	Wang <i>et al.</i> , "Lipid Clearing Agents in Steroid-Induced Osteoporosis," J FORMOS MED ASSOC (1995) 94:589-592

EXAMINER:

DATE CONSIDERED:

EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.

Form PTO-1449 INFORMATION DISCLOSURE CITATION IN AN APPLICATION <i>(Use several sheets if necessary)</i>		Docket Number 432722002623	Application Number 09/695,807
		Applicant	Gregory R. MUNDY <i>et al.</i>
		Filing Date October 23, 2000	Group Art Unit 1646
		Mailing Date July 10, 2001	

94.	Wojcik <i>et al.</i> , "Ubiquitin-Mediated Proteolysis Centers in HeLa Cells: Indication from Studies of an Inhibitor of the Chymotrypsin-Like Activity of the Proteasome," EUR J CELL BIOL (1996) 71:311-318
95.	Wozney, "The Bone Morphogenetic Protein Family as Osteogenesis," MOLEC REPROD DEV (1992) 32:160-167



EXAMINER:	DATE CONSIDERED:
EXAMINER: Initial if citation considered, whether or not the citation conforms with MPEP 609. Draw a line through the citation if not in conformance and not considered. Include a copy of this form with next communication to applicant.	